Process development H_2O_2 decontamination

Summary

- Systems
- Principle
- Tool
- Steps in the Cycle Development process
- Conclusion

3 possibilities of decontamination with H_2O_2 …

SIS 700

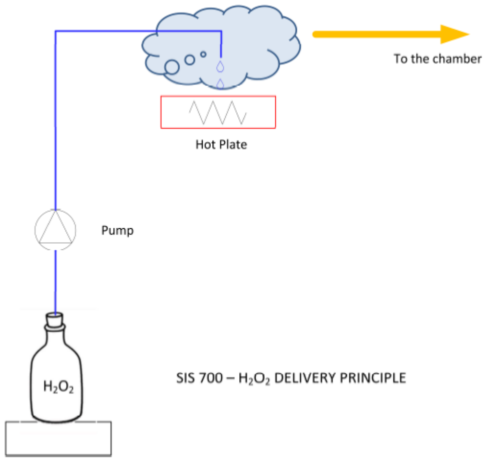
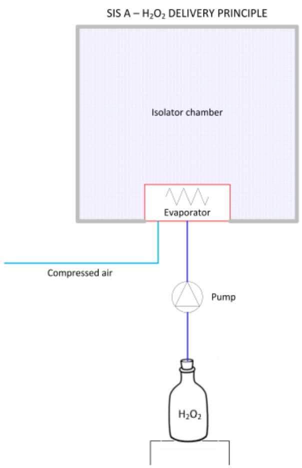


Figure 2: SIS700 – H_2O_2 delivery principle

SIS A



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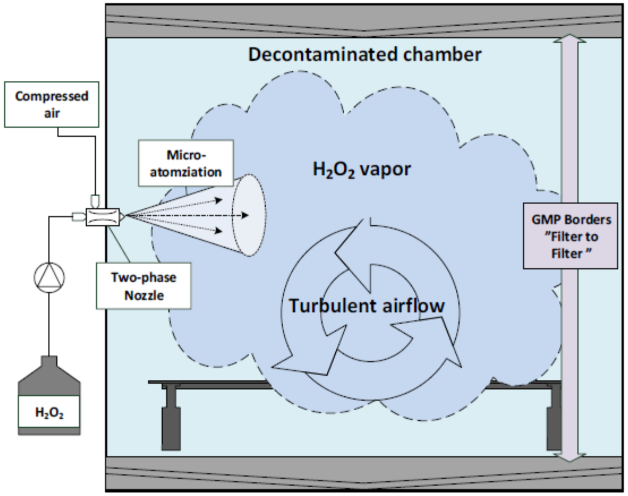
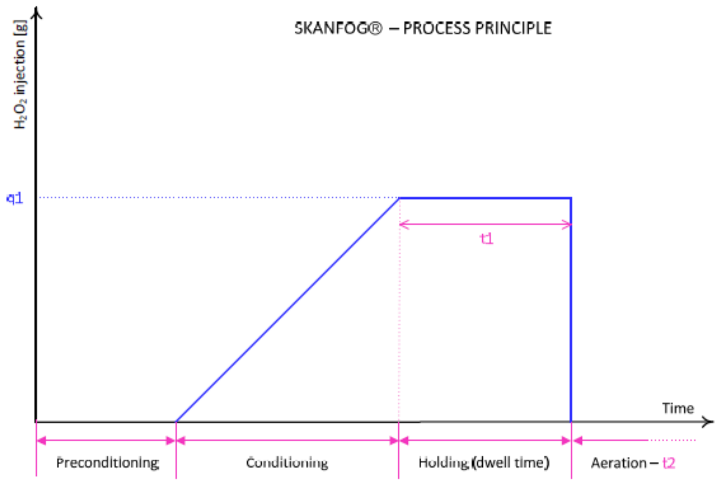
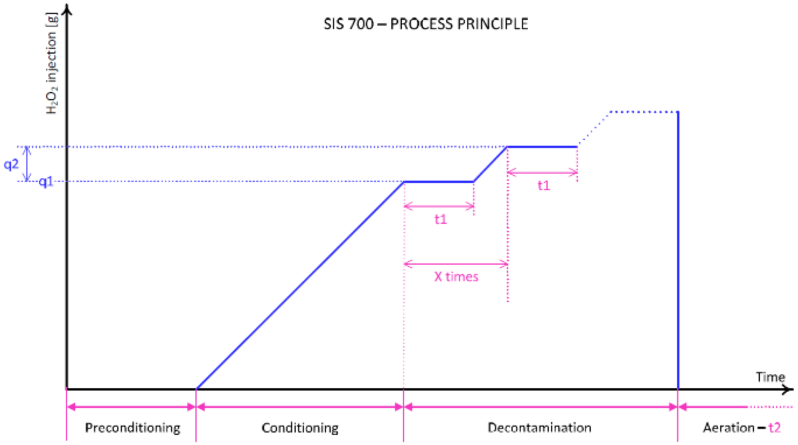


… 1 unique process

- Definition of loading pattern
- Determination of H_2O_2 quantity just enough to kill
- Confirmation of effectiveness of the cycle (sustained effect)
- Determination of worst case positions
- Total Kill
- Safety margin

Principle of decontamination



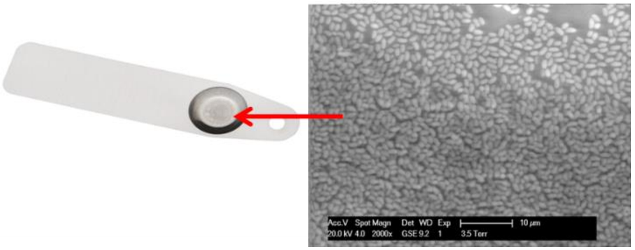


Principle of decontamination

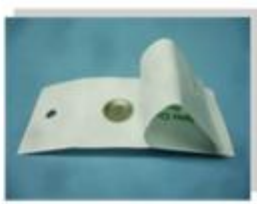
- **Conditioning** is defined as the injected H_2O_2 amount enough to achieve a total kill (10 Spore Log Reductions - SLR) in the loaded chamber (within sterility boundaries).
- **Holding time** is defined as an extra contact time long enough to achieve a total kill in the entire isolator (hidden parts) without H_2O_2 injection.
- **Aeration time** is defined as the time needed to reach the required residual H_2O_2 level in the enclosure.

Tool for the inactivation process

- Biological Indicators (BI)
  - Defined / required test organism
  - Defined / required initial population
  - Carrier material
  - Primary Packaging
  - Defined resistance against a specific inactivation method



Disc in Primary Packaging



Spoon in Primary Packaging

Steps in the Cycle Development process

Prerequisitie s

- IQ / OQ performed without any open issue impacting the CD.
- Clean system.
- Available User Requirement Specification (URS)
  - Definition of the boundaries of the system.
  - Required residual H_2O_2 concentration after the end of aeration phase.
  - Germ reduction ensured by the decontamination cycle (Spore Log Reduction).
  - Maximum duration of the Decontamination Cycle.
- Loading pattern(s) / materials.

Steps in the Cycle Development process

Prerequisities

- Unique process for each isolator
  - Your environmental conditions
  - Your setup for the routine process
  - Your requirements to the documentation

Steps in the Cycle Development process

Steps in the process in a chronological order

- Definition of loading pattern
- Determination of the total kill time
- Temperature mapping (optional)
- Relative humidity mapping (optional)
- Chemical indicator mapping (optional)
- Definition of worst case locations
- Worst case study
- Determination of aeration time

Steps in the Cycle Development process

Definition of Loading Pattern

- Attention should be paid to:
  - Shadow on other element of the load, the system.
  - State of the load (T°C, absorption, adsorption, etc.).
  - Airflow pattern
  - Convenient space between loaded elements
  - Cleanliness (recommended)

Steps in the Cycle Development process

Definition of loading pattern

Steps in the Cycle Development process

Steps in the process in a chronological order

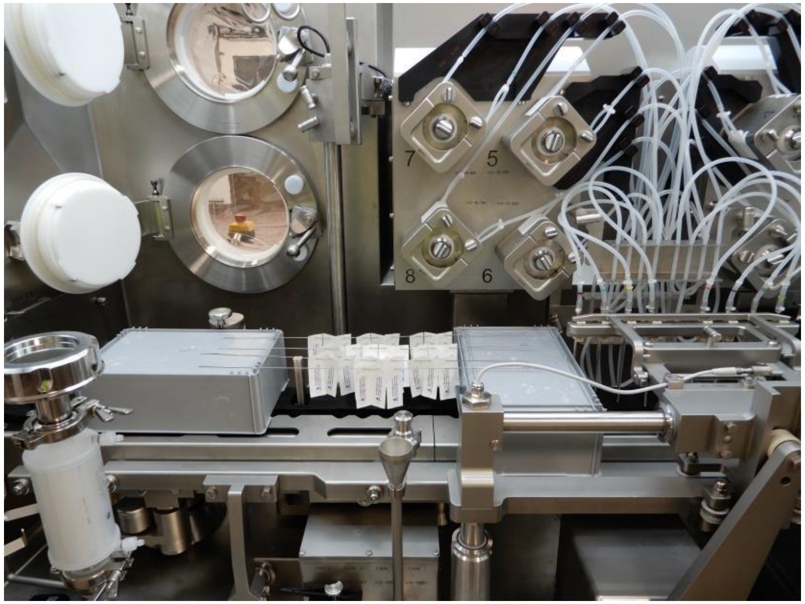
- Definition of loading pattern
- Determination of the total kill time
- Estimation of the homogeneity of the distribution
- Temperature mapping (optional, system-dependant)
- Relative humidity mapping (optional, system-dependant)
- Chemical indicator mapping (optional, system-dependant)
- Definition of worst case locations
- Worst case study
- Determination of aeration time

Steps in the Cycle Development process

Definition of Total Kill Time

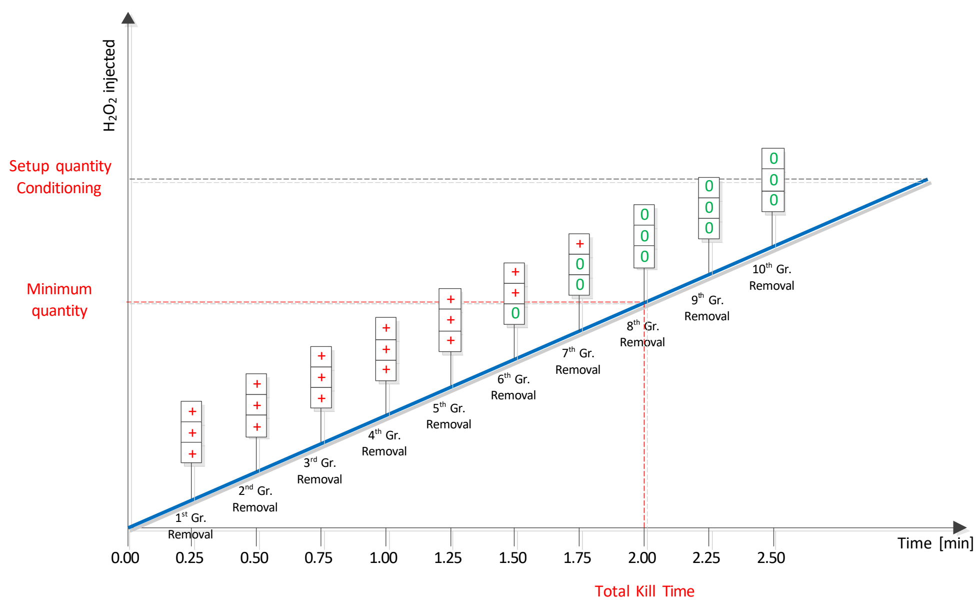
- "i" groups of "n" BIs per group are exposed in the middle of the loaded chamber (best place), at the beginning of the cycle. Each "d" minute(s) one group is removed.

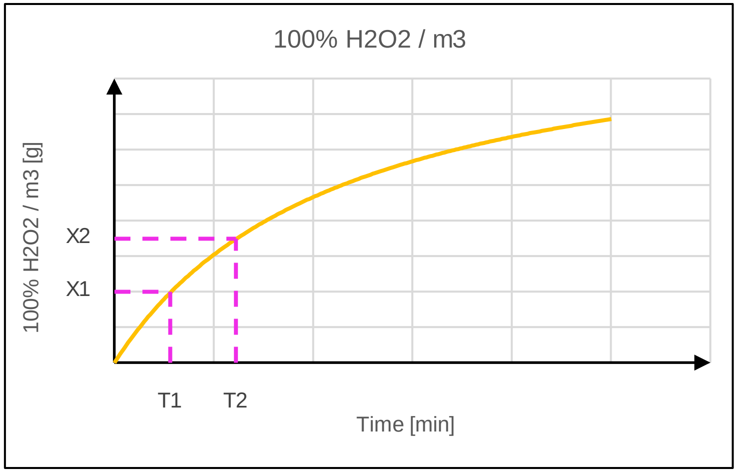
- After incubation and reading of the BIs, the Total Kill Time [min] is defined as the first time, where no growth is observed.



Steps in the Cycle Development process

Definition of Total Kill Time (example)





Steps in the Cycle Development process

Steps in the process in a chronological order

- Definition of loading pattern
- Determination of the total kill time
- Temperature mapping (optional)
- Relative humidity mapping (optional)
- Chemical indicator mapping (optional)
- Definition of worst case locations
- Worst case study
- Determination of aeration time

Steps in the Cycle Development process

Steps in the process in a chronological order

- Definition of loading pattern
- Determination of the total kill time
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- Relative humidity mapping (optional)
- Chemical indicator mapping (optional)
- Worst case study
- Determination of aeration time

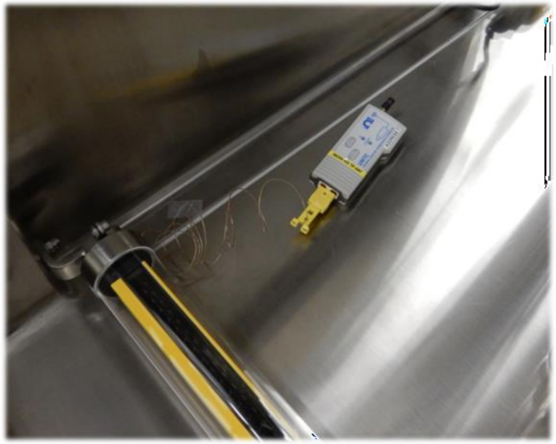
Steps in the Cycle Development process

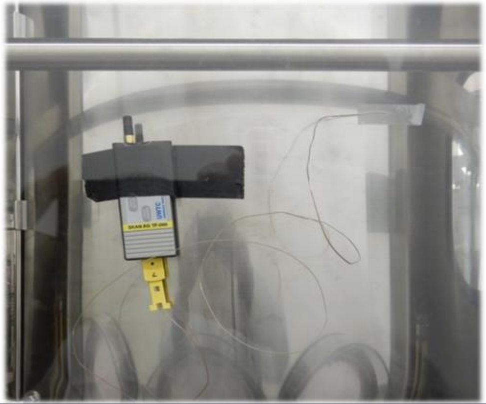
Temperature / Relative humidity mapping

- Evaluation in conditioning and holding time
- No acceptance criteria
- Extreme values do not represent a fail! They are atypical and represent worst case positions that should be challenged with BIs on a regular basis (initial qualification and requalification).

Steps in the Cycle Development process

Temperature / Relative humidity mapping



Steps in the Cycle Development process

Temperature / Relative humidity mapping

Steps in the Cycle Development process

Steps in the process in a chronological order

- Definition of loading pattern
- Determination of the total kill time
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- Chemical indicator mapping (optional)
- Definition of worst case locations
- Worst case study
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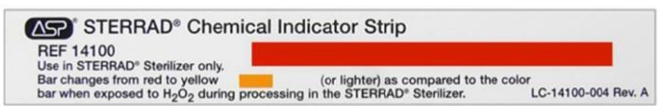
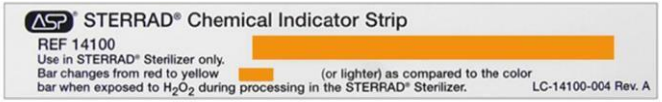
Steps in the Cycle Development process

Chemical indicator mapping

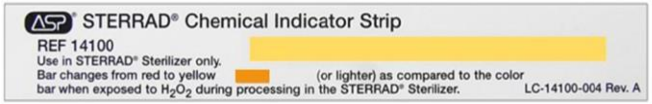
- Qualitative evaluation of the homogeneity of the distribution of H_2O_2 “everywhere” in the isolator.
- Evaluation is made through the color change of H_2O_2 sensitive chemical indicator
- Shade for reading is as follows (ASP 14100):



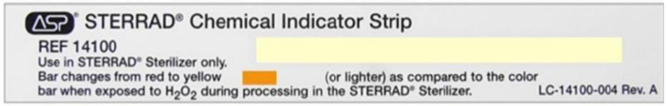
Not exposed or not reached by H_2O_2 vapor / gas



Effective action of H_2O_2 vapor / gas at this location



Presence of H_2O_2 vapor / gas at this location. Relative humidity to be increased



H_2O_2 ppm too high. T°C too high and/or relative humidity too low. Poor cycle.

Steps in the Cycle Development process

Chemical indicator mapping

Steps in the Cycle Development process

Steps in the process in a chronological order

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- Chemical indicator mapping (optional)
- Definition of worst case locations
- Worst case study
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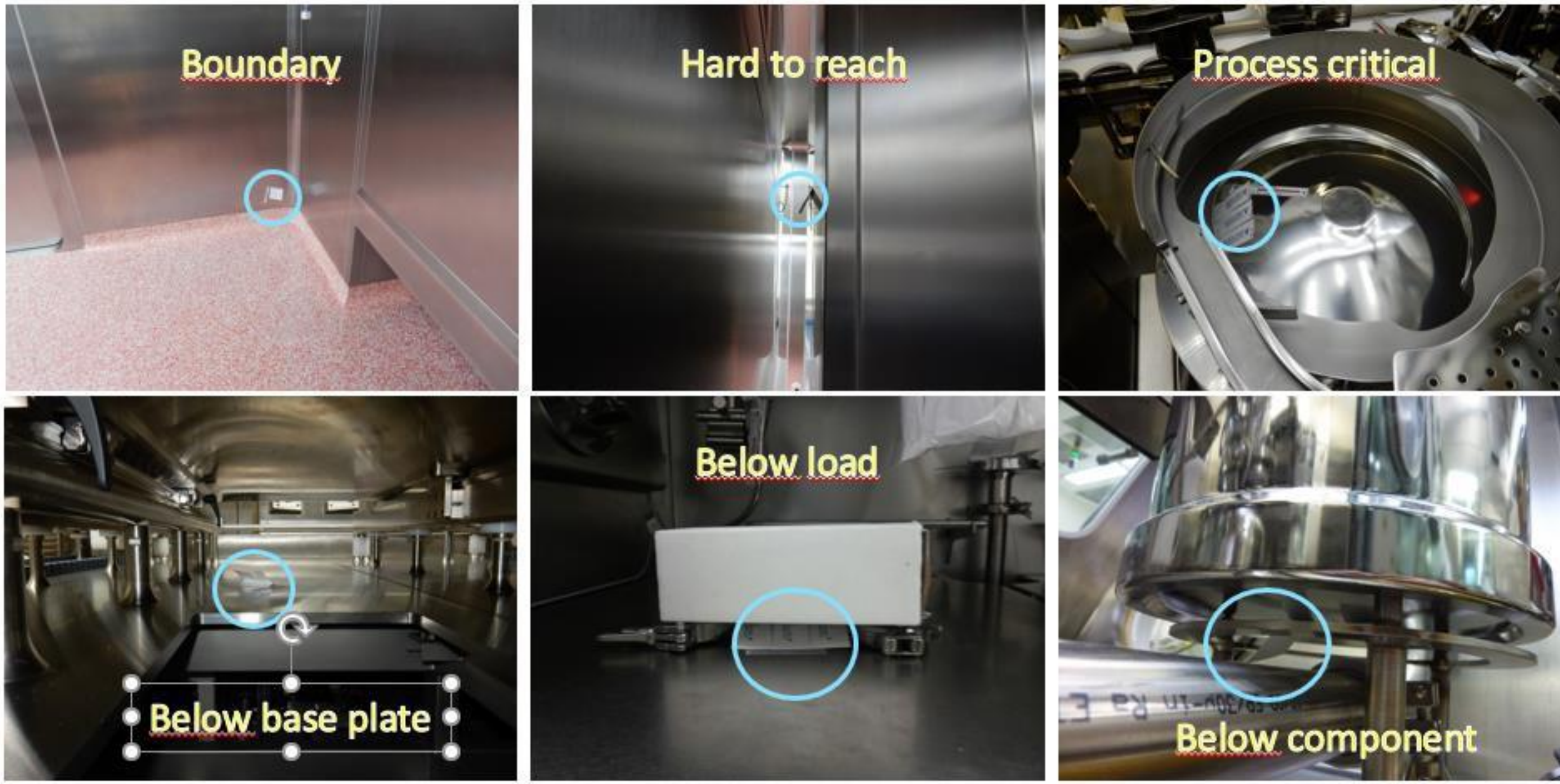
Steps in the Cycle Development process

Worst Case Positions - assessment criteria

Filling Line	Position No.
1. Edges of system enclosure (decontamination boundaries)	02; 03; 04; 05; 06; 07; 08; 13; 14; 15; 16; 17; 18; 23; 24; 28; 29; 30; 31; 32; 33; 34; 35; 38; 50; 51; 76; 77; 78; 79; 80; 81; 82; 83; 99; 100; 101; 102; 103; 104; 105; 106; 112
2. Potential difficult distribution of H_2O_2	01; 09; 10; 11; 12; 19; 39; 42; 43; 88; 89; 94
3. Under / on components of the system / parts of loading	20; 25; 26; 27; 36; 41; 58; 66; 84; 90; 92; 107; 108; 109
4. At gloves or sleeves	46; 47; 48; 49; 72; 74; 75; 95; 96; 97; 98; 113; 114; 115; 116
5. Process critical position	40; 44; 65; 67; 69; 70; 93
6. Near air entrances or air exits, decontamination loop	22; 37; 45; 60; 71; 87; 110
7. High / low temperature or relative humidity	62; 63; 68
8. Movable parts of the machine	52; 53; 54; 55; 56; 57; 61
9. Homogeneous and geometrical distribution	64; 85; 86
10. Customer specific request	N/A

Steps in the Cycle Development process

Worst Case Positions - examples



Steps in the Cycle Development process

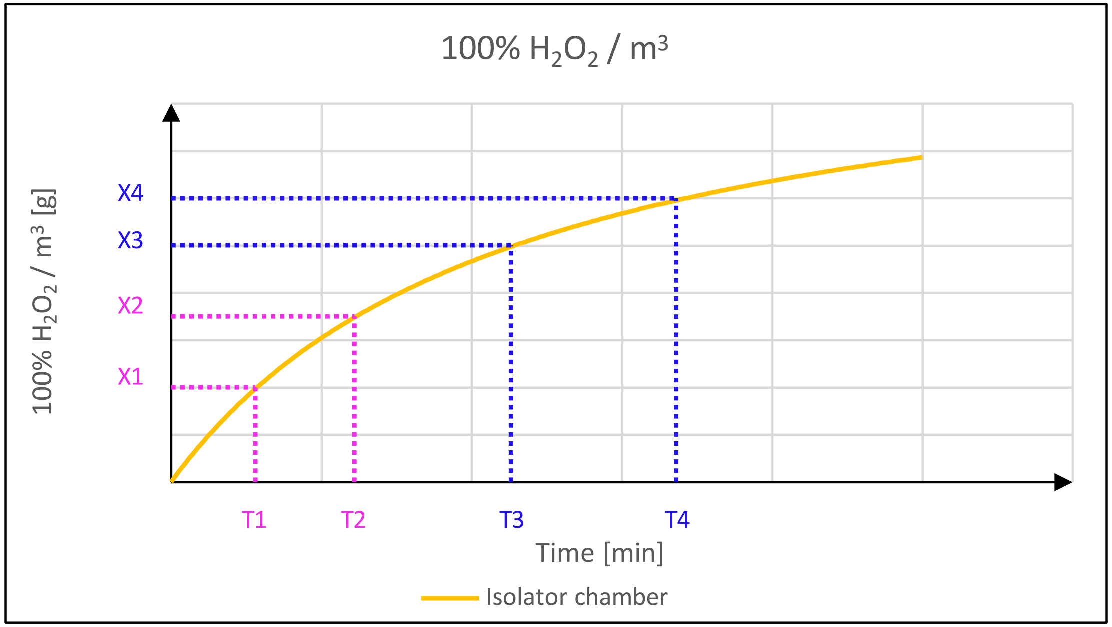
Worst Case Positions - operation

- Once the total kill time is defined and the homogeneity of the distribution is proven, the worst case study is performed with parameters calculated from the results of the "Homogeneity of the Distribution" testing.
- All worst case locations are challenged with multiple BIs per position. In case of positive BIs, this allows to estimate how far the cycle is from the required SLR (Spore Log Reduction).
- The objective of this step is to define the "just needed power" to kill all the BIs exposed.

Steps in the Cycle Development process

Worst Case Positions - operation

- If random growth occurs, then the effectiveness of the cycle has to be slightly increased.



Steps in the Cycle Development process

Steps in the process in a chronological order

- Definition of loading pattern
- Determination of the total kill time
- Estimation of the homogeneity of the distribution
- Temperature mapping (optional)
- Relative humidity mapping (optional)
- Chemical indicator mapping (optional)
- Definition of worst case locations
- Worst case study
- Determination of aeration time

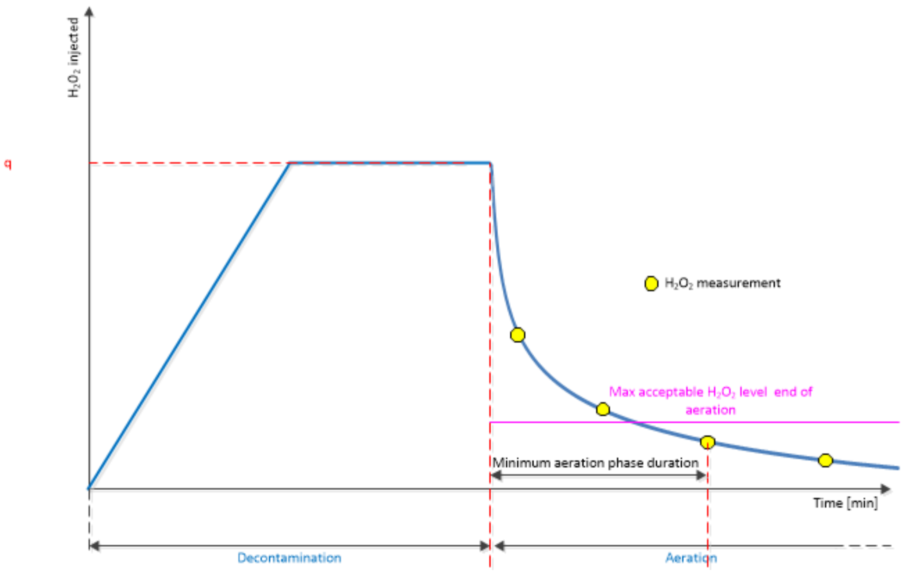
Steps in the Cycle Development process

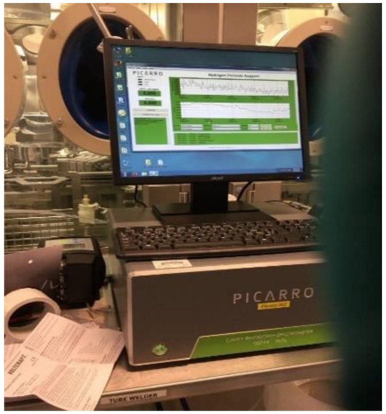
Determination aeration time - operation

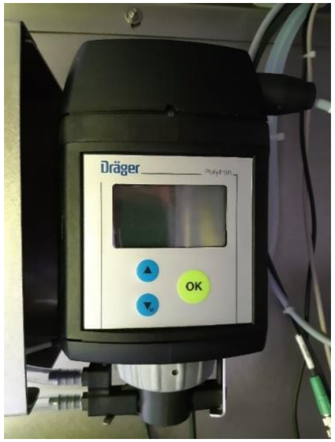
- The minimum aeration time is the time needed to decrease the H_2O_2 level in the chamber to an acceptable level for the process, taking also health and safety in consideration (transfer airlock).
- The residual H_2O_2 measurement device should be adapted to the maximum acceptable H_2O_2 level at the end of aeration. It can be an in line / off line measurement (Dräger LC sensor, Picarro) or a manual sampling (Dräger tube).
- Ambiance conditions in the system should be evaluated and compared to the technical specifications of the measurement device.

Steps in the Cycle Development process

Determination aeration time





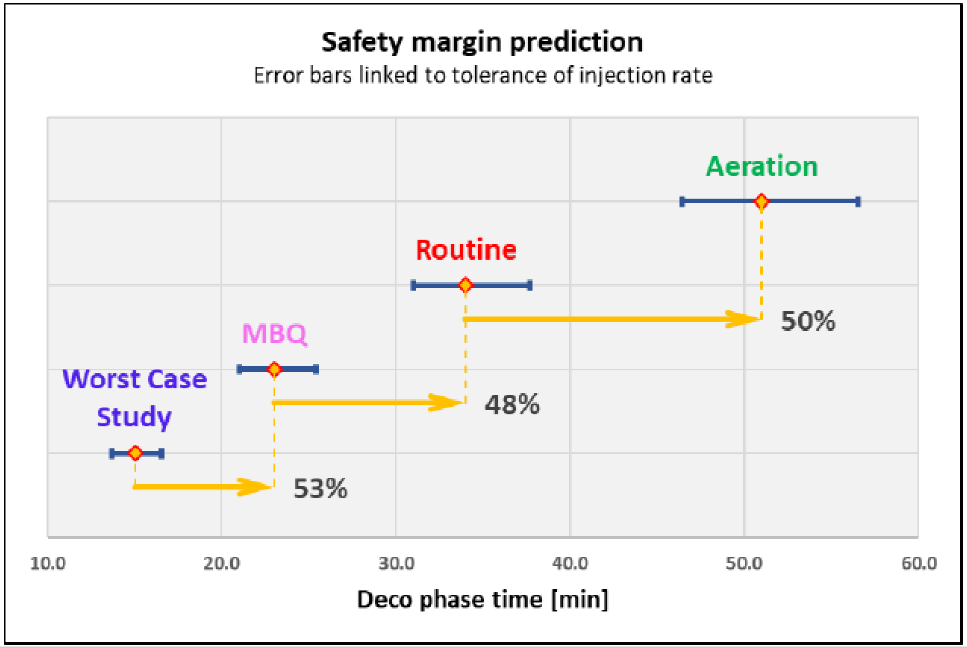


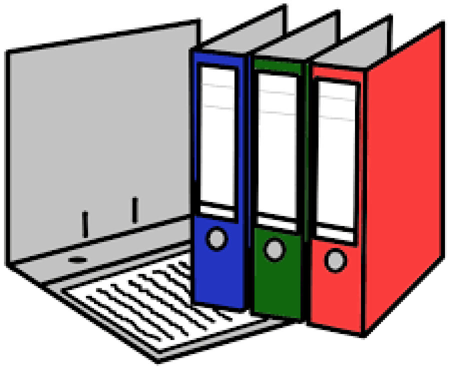
Steps in the Cycle Development process

Determination aeration time - results

- The first measurement below the maximum acceptable level of H_2O_2 at the end of aeration defines the minimum aeration time for the considered loading pattern.
- The final aeration time that will be taken into account is the time that gives conform results for all loading patterns challenged (longest aeration phase duration).

Conclusion


Safety margin prediction
Error bars linked to tolerance of injection rate
Aeration
Routine
MBQ
Worst Case Study
50%
48%
53%
10.0
20.0
30.0
40.0
50.0
60.0
Deco phase time [min]



And then…….

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strategic Product Management